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A Clinical Study of the Action and Uses of
Caffeine and Convallaria Majalis
as Cardiac Tonics.

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A Clinical Study of the Action and Uses of Caffeine and Convallaria Majalis as Cardiac Tonics.

—BY—

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Until very lately many of us were accustomed to regard digitalis as the essential, nay almost the only real stimulant, or tonic of the heart. True it is, we consider alcohol a powerful general stimulant, and incidentally recognize that it gives the heart renewed power.

In ether and ammonia we have, also, diffusible stimulants of considerable value, but their action is evanescent and is not to be relied on, if a continued or specific effect upon cardiac contractility is required.

In iron, quinine and nux vomica, or its alkaloid, strychnine, we have three very powerful corroborants. They restore appetite, make blood of better quality, add to muscular vigor, and rehabilitate in a notable degree the general system. At the same time they strengthen and regularize cardiac pulsations, but this latter result is obviously only a part, though at times an important one, of their general influence for good.

In coca, also, we have a powerful stimulant to the economy that frequently will strengthen, or give tone to the nerves in a rapid manner, that no other drug with which I am familiar, can accomplish.†

In belladonna, we have, however, the only drug which has hitherto seemed to me ever to take the place, even in a moderate degree, of digitalis in its direct tranquilizing, and at the same time strengthening effect, upon the heart. But belladonna appears to influence, especially, the cardiac plexuses and the intra-cardiac ganglia, and not to give immediate power to cardiac muscular fibre as digitalis does. In severe collapse,‡ resulting from inflammation and other diseases of abdominal organs, and especially in cholera, we have learned to admit its very great value, and how much benefit we may derive

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† I have repeatedly felt this effect of Mariani's wine of coca on myself, when extremely fatigued from overwork or want of sleep. The wine of Mariani is, I believe, one of the best preparations, on account of the great care exercised by its maker.

‡ Philadelphia Med. Times, Feb. 2d, 1878, p. 198.

from its timely exhibition, but in acute or chronic heart disorders of the kind we encounter habitually, belladonna must not be relied upon to the exclusion of digitalis. As an adjunct in a prescription to give tone and power to the heart, it should be judiciously employed, and frequently we shall recognize manifest good effects resulting from its use. Even when employed alone, I have observed a number of cases in which palpitations were diminished, and the cardiac pulsations rendered more regular and stronger. But once let the heart commence to fail evidently in its rôle as an ever-acting force pump; should its cavities dilate never so little; should secondary hypertrophic compensation following organic lesion of valves, or orifices begin to fail; should co-ordinate nerve control by the vagi, the sympathetic, or the intra-cardiac ganglia, be manifested by obstinate or excessive palpitations, quiverings, irregularities, or intermittences in the beats, and at once we would recur, whatever else we do, to the internal use of digitalis in small, or large, rare, or frequently repeated doses. Very often it would help us in our time of need, help us as possibly few medicinal agents ever will, to give strength and regularity to the circulatory function, when it was fast showing signs of weakness and asystolism. Occasionally, however, we are disappointed in its employment; it has been unable to respond to our anticipations of its good work, and where we had relied most confidently, there we were soon prepared to acknowledge we had encountered disappointment. Possibly on this account we were glad to welcome any drug, or drugs, which should fill a lacuna already appreciated. Or even if we doubted that a gap could be made whole, we were pleased to know that there were other remedies of value in cardiac therapeutics than those to which we have referred. Be that as it may, within the past year, three new drugs have claimed our attention as cardiac tonics: The first is caffeine; the second convallaria majalis, or its glucoside, convallamarin; and the third, nitro-glycerine.* It has seemed to me profitable, even at this early date, to present to a body of busy practitioners something of what is actually known in regard to the nature, action and uses of these three agents, and also, to accompany my remarks with records of some personal cases and the obvious deductions which can be made from them.†

* This drug is administered under the name of liquor glonoin, which is a solution of nitro-glycerine of such strength that one drop represents one one-hundredth grain nitro-glycerine, the usual dose, to be cautiously increased according to circumstances.

† I had at first intended to make a tolerably complete study of nitro-glycerine and approximate the action of this remedy with that of caffeine and convallaria. Unfortunately my cases, with two exceptions, have not hitherto seemed to require its use, and I am now obliged to present my paper before you without completing it in this regard, as I so much desired. I will simply add for those who may for the moment fail to recollect these facts, that nitro-glycerine was discovered by M. Sobrero in 1847, and further investigated by Railton and De Vrij. It has been recommended for various forms of nervous diseases by A. G. Field, M. D., of St. George's Hospital, London, and brought to the attention of the medical profession in New York by Dr. Wm. A. Hammond, who says of its therapeutical uses, "From the action of nitro-glycerine it is to be expected that the drug would be of value in those instances in which it was desirable to stimulate the circulation and increase the amount of inter-cranial blood."

Caffeine, or citrate of caffeine, as it is improperly termed,* is no new remedy. For a long time its diuretic action has been familiarly known, but not until the labors of Gubler, Lewis Shapter and Leech was the attention of the medical profession specially directed to it as a cardiac tonic and regulator. Since the contributions of Gubler, various articles have appeared in which its action in this direction, or in promoting diuresis, has been most favorably spoken of. A valuable study in the *Edinburgh Medical Journal*,† by David J. Brakenridge, "On the Action and Uses of Citrate of Caffeine as a Diuretic;" another by Lépine in the *Lyon Médicale*;‡ a third by Huchard in the *Bulletin Général de Thérapeutique*;§ and a fourth by Milliken (F. H.) in the *Philadelphia Medical Times*, and entitled, "Citrate of Caffeine in Cardiac Dropsy,"§ form the sum of what has been hitherto discovered in regard to the clinical employment of this drug. All of these writers recognize in caffeine a useful and valuable addition to our therapeutic arsenal. As a cardiac tonic, Lépine considers it, with somewhat different merits, the equal of digitalis. Huchard does not bestow such high praise as this, but is willing to agree that when digitalis fails to produce beneficial effects, we shall act wisely in turning to caffeine in the hope of obtaining relief for our patient. Caffeine in moderate doses at first slows the heart,** afterwards the cardiac pulsations are prone to become more rapid. In the beginning the cardiac beats are stronger and more regular. This effect may be kept up for quite a long time, or ultimately may be lost in part. Its action on the respirations is not so evident. However, it appears to make them deeper and of longer duration. Its influence over dropsy is very great at times; again, it is quite inert in this regard. Whenever the dropsy is dependent simply upon cardiac failure, caffeine invariably increases the secretory function of the kidneys; the quantity of urine passed in a given time is very largely augmented, and in a corresponding degree the infiltration of tissues subsides. Whenever the anasarca is an expression of acute parenchymatous renal degeneration, caffeine has no diuretic action whatever. It would seem that this action belongs, in caffeine, to its direct influence upon the glandular renal epithelium and is not exerted through the vessels of the kidney. Brakenridge has, indeed, shown by several reported cases, that in the early stages of acute parenchymatous nephritis the diuretic action of caffeine was completely nil. At a later stage of this affection it not only increased the quantity of water eliminated by the urine, but also notably augmented the excretion of urea and other urinary solids. The

*In this connection I would state that in a written communication to me from Chas. Rice, Esq., Pharmacist to Bellevue Hospital, in date of Nov. 17, 1882, it is affirmed that there is no chemical combination of a permanent character known as citrate of caffeine. What is sold under this name is usually nothing but caffeine. In some rare cases where citrate of caffeine has been asked for, the dispenser has simply made a combination of very temporary nature, between citric acid and caffeine, in order to supply a demand, which is probably an expression of ignorance in regard to the essential nature of the drug called for.

†July and August, 1881.

‡Juillet, 1882.

§30 Août, 1882.

§February 25, 1882.

**According to Huchard, caffeine renders the cardiac action more rapid at first.

quantity of urea excreted was particularly and greatly increased whenever its eliminated quantity in a given time had fallen short of the normal amount before caffeine was taken. Brakenridge, however, has become convinced that digitalis and caffeine are complimentary of one another in their diuretic action, and further, that when given at the same time they exert a far more powerful diuretic action than when given each drug by itself. This is fully explained by the well-known fact that digitalis acts as a diuretic by increasing blood pressure in the general and local arterial system as well as by increasing the amount of blood-flow in a given time through the kidneys. Caffeine, on the contrary, has an elective action upon the secretory power of the glandular renal epithelium, and their secretory power is at times very much augmented without the slightest increase being manifested in the blood pressure, and when the radial pulse-beat is rapid, feeble and depressible, not to say quite irregular. It is proper to remark here, that it is only with doses larger than Brakenridge employs that Lépine, notably, pretends to get the therapeutic effects of caffeine upon the heart action in the way of slowing and strengthening it. Over digitalis, caffeine has certain evident advantages :

1. It has no tendency to cumulate in the economy and hence to occasion poisonous effects.*
2. It acts with greater rapidity than digitalis. In certain cases of asystolism, when life is imminently endangered, this property may be of great value.
3. It rarely or never disagrees with the stomach, when it has diuretic effects, or in any way causes symptoms of a dyspeptic character. This may and probably does depend in a large measure upon its rapid and easy elimination from the body, especially through the kidneys, unless acute parenchymatous nephritis be present. Its disadvantage, in certain instances, is to stimulate the brain too actively and thus to occasion persistent wakefulness and other nervous symptoms. Moreover, its cost is very considerable. To be effective, it must be given in relatively large doses from the beginning.† Six grains a day is the smallest amount that will show any special elective action, and this amount may be rapidly increased to 20, 25, 30, or in very exceptional instances, to 35 grains a day. It should be given in capsule, or mixture with syrup of orange, or some other agreeable vehicle. It should be given, also, in divided doses, so that its action may be continuously kept up and not cause stomachal rejection. As I have already stated, it is

*Of course I refer here to ordinary, or even large doses, relatively, of caffeine. On one occasion, last summer, I was called to see a lady who, after taking by mistake, as much as a teaspoonful of caffeine, showed evident signs of poisoning. These signs were great mental excitement, unequal action of the heart and cold extremities, followed soon by prolonged wakefulness, not influenced much by moderate doses of opium.

†This is Lépine's and Huchard's opinion. Brakenridge, on the contrary, affirms he can get all the diuretic effects possible by giving grs. iij, doses t. d. s., in pill, or solution.

rapidly eliminated from the economy. Tanret has given a formula for its hypodermic use, and vaunted its exhibition after this method.*

Personally I have given caffeine to the following cases with good results :

Case 1.—A young woman, about 25 years of age, in the fourth week of a tolerably severe case of typhoid fever. At that time the temperature in the axilla was still 103 degrees Fahr. in the evening. The bowels were moderately loose, the heart beats were extremely feeble, muffled and somewhat distant; the pulse was dicrotic, depressible and irregular; there was marked adynamia, with dry, rather brown tongue on dorsum and a condition of cerebral apathy very marked. In fact, the patient was usually in a semi-somnolent state from which she was aroused not without addressing her remarks very forcibly and in an elevated tone. She was taking 12 ounces of brandy in the 24 hours, and 10 grains of quinine. The brandy was dropped to six ounces, the quinine suppressed, and two grains of caffeine were given every two hours in mixture. This medication was only continued two or three days. During that time the pulse became decidedly stronger and more regular, the cardiac pulsations more forcible and the patient awakened from her condition of previous lethargy. The effects of caffeine on the urine in this case were not noted.

Case 2.—*Diagnosis* : Cardiac hypertrophy; aortic stenosis. C. S., single, waiter, mulatto.

October 17, 1881.—Complains of tightness over the chest anteriorly since yesterday; looks pale and somewhat jaundiced; constipated.

Physical Examination : Reveals considerable hypertrophy of the heart, with well-marked, rather harsh blowing murmur at the base accompanying the first sound.

R Pil. podophyll. co.

(Gr. $\frac{1}{4}$ podophyllin in each pill.)

S. One pill to be taken every night.

R Tinct. belladonnæ,
Tinct. nucis vomicæ, $\overline{\text{ss}}$ gtt. ij,
Mist. potass. citratis, $\overline{\text{ss}}$.

M. S. Take every six hours.

October 24, 1881.—Has annoying cough.

R Mist. glycyrrhiz. co., $\overline{\text{ss}}$ ij,
Sp. chloroformi, $\overline{\text{ss}}$ ss.
Sp. ammonii aromat., $\overline{\text{ss}}$ j.

M. S. A teaspoonful every two hours.

*The ordinary preparations of caffeine are unsuitable for hypodermic use on account of their slight solubility in water. Owing to an analogy which exists in coffee where caffeine is found as a double salt of caffeine and potassium combined with an acid resembling salicylic acid, Tanret was led to make a combination between caffeine and salicylate of soda. The salicylate contains 61 per cent. of caffeine, and has been injected subcutaneously without causing the slightest irritation.—*Medical Record*, Jan. 6, 1883, p. 9.—*Schmidt's Jahrbücher*, No. 7, 1882.

October 20, 1882.—Complains of constricted feeling over the chest in front. On applying ear to the thorax I am able to distinguish the same kind of blowing murmur as heard one year previously.

R Caffeine, gr. ij.

S. Take in capsule every four hours.

October 26.—Took medicine during four days. Pain in chest disappeared. He felt slight pain over hip and left side. Caffeine increased bulk of urine in a marked degree; did not remark that it made him breathe more easily.

Case 3.—*Aortic Stenosis. Frequent Attacks of Vomiting*: Mrs. K., widow, 60 years of age, suffering from repeated attacks of nausea and vomiting during several years. The cause of these attacks was undetermined. At first it was thought they were occasioned by a simple catarrhal gastritis which itself was under the dependence of errors of diet, mental anxiety, and excessive fatigue on the part of one with a feeble constitution. This hypothesis was found to be erroneous, inasmuch as treatment instituted from this point of view proved but temporarily serviceable at any time. Usually it was of no use whatever. The urine was examined repeatedly, but no abnormal change could be found which could lead any one to suspect disease of the kidneys. A slight error of refraction, due to age, was rectified by wearing suitable glasses. Aortic stenosis was discovered, and as heart action was weak, small doses of digitalis were prescribed. No good effects followed either as regards the action of the heart or stomachal troubles.

October 20, 1882.—Constant nausea during several days past. Two attacks of vomiting with rejection of the entire contents of the stomach.

October 21.—Three vomiting attacks in the afternoon; pulse weak; no irregularities or intermittences; depressible; no perceptible murmur at heart; rather slow, feeble action.

October 22.—

R Caffeine, gr. ij.

S. Take every four hours.

October 28.—Has not had another attack of vomiting or any feeling of nausea; second night after use of remedy had noises in the head which resembled the escape of steam from a boiler; no increase in quantity of urine; noises in head did not repeat themselves on October 25th; felt stronger and better since that date.

On October 27th did not take caffeine.

To-day (Oct. 28th) moderate rough bruit at base of heart, synchronous with first sound. Heart action more forcible; pulse somewhat less depressible, although not yet of normal strength.

Note—Case seems to be one of recurrent and periodic attacks of vomiting, probably due to congestion of stomach, secondary to chronic cardiac disease. (Aortic stenosis.)

November 23, 1882.—Has been taking two-grain capsules of caffeine every two hours (?) and has not had an attack of vomiting in two weeks.

Case 4.—*Asystolic*: Treated at different times with caffeine, digitalis and convallaria; no pronounced abnormal murmur generally; improvement. (Careful notes taken during two months.)

Mrs. W. M., widow, 49 years of age. Complains, for several years, of palpitations and shortness of breath on slight exertion. A thin, spare woman, mother of several grown children, a school-teacher by profession. Last winter (Dec. 1881) I treated her for an obstinate attack of bronchitis which lasted several weeks, and seemed to be kept up partly by deficient heart power. Improved and got finally well, by the repeated use of belladonna, nux and digitalis in small doses, several weeks continued. Has been well during past summer.

October 20, 1882.—About three weeks ago taken with more oppression than usual, and was unable to rest quietly at night on account of dyspnœa. Considerable anasarca at that time of trunk and lower limbs. Again improved on small doses of digitalis. Finding her condition after a few days not as much improved as I desired, viz.: although oedematous condition had in part disappeared, she complained still of short breathing and restlessness at night. Moreover there was insufficient excretion of urine, not more than 1 pint in 24 hours; no albumen; normal specific gravity. I put her (Oct. 16) on 2 grains caffeine every two hours with a little syrup and aq. menth. pip.

October 9, 1882.—I found heart action stronger, less rapid, and more regular in rhythm. (There was no murmur now or before, properly speaking, although the first sound was prolonged and not as clear as normal.) Pulse weak 90 per minute; urine far more abundant; rests better; less dyspnœa; oedematous swelling of body almost disappeared; appetite still very poor; repeat caffeine 2 grains every 4 hours.

October 14, 1882.—Still continues better; last two days only taken 3 or 4 doses in 24 hours.

October 18, 1882.—Finds caffeine at times relieves her breathing very much; at times, it does not. Not quite as well as she was last time; suffers more from dyspnœa at night and absolute inappetence. Return of *asystolic*:

℞ Tr. nucis vomicæ, gtt. v
Tr. belladonnæ, gtt. v
Mist. amygd., 3 ij.

M. S. Every four hours.

October 19, 1882.—Has slight hacking cough; thinks she caught a cold in nursing an ill son at night. Repeat medicine.

October 21, 1882.—Complains still of cough:

℞ Ammon. carb., gr. xxx
Tr. nucis vom., gtt. xxv
Tr. digitalis, gtt. xv
Syrupi acaciæ, ʒj
Aquæ, ad. ʒ iij.

M. A teaspoonful every two hours in a little water.

October 29, 1882.—Cough nearly gone, breathing improved, but still obliged to be propped with several pillows at night in order to sleep; says that first mixture with caffeine helped her breathing most; legs have been very œdematous last few days, abdomen increased in size, (due to serous effusion).

R Bandaged legs,
Pulv. scammon co., gr. vij.

S. * Every three hours.

R Bitartrate of potash lemonade, 3 ij-Oj
Acet. pot., gr. x.

Every two hours. (Says that urine is deficient in quantity.)

November 11, 1882.—Complains of cough and dyspnœa; slight frothy sputa; legs more swollen; small quantity of urine; few subcrep. râles in chest, especially in front, face pale and puffy; eats more.

R Fl. ext. convallariæ majalis, gtt. 5.

Every three hours, increase to gtt. 10, if suits. Wet pack to make sweat; has considerable diarrhœa following use of scammony powders. Asystolie marked; pulse regular and quite good as regards strength.

November 12, 1882.—Finds convallaria promotes pleasant sleep; whenever she takes it, sleeps quietly; does not cause nausea; helps her breathing; she breaths more easily; her cough about the same with blood streaked sputa, during last 24 hours.

R. Repeat convallaria, and apply Stokes' lin. over chest.

November 16, 1882.—Leg (left) very much swollen and painful; worse now than ever been since she had phlegmasia in it many years ago; right leg very slightly swollen; heart action stronger and somewhat slower and more regular; still, however, marked asystolie; says that convallaria gives more relief to her breathing than any drug she has tried; continues to make her sleep; took 7 gtt. last night at a time, instead of five, slight dry, hacking cough; appetite poor.

Repeat convallaria; poultice of digitalis leaves to leg. Hot air bath daily (took a hot air bath last two days and thinks the perspiration helped her, although it was not very free).

Nov 23, 1882.—Better than yesterday; breathes better and less cough; face has bloated appearance; moderate effusion into left pleural cavity; left leg much swollen and painful; appetite very poor; took hot air bath at Windsor baths yesterday; tried her strength very much; limbs (lower) seem more swollen since upper portion of body perspired well; not lower.

November 19.—Ordered the following :

R Sp. æth. nitrosi,
Infusi digitalis, ℥ss.
Liq. ammon. acet., ℥iij.

M. S. 3 ij. every two hours.

This mixture did not increase quantity of urine notably, but rendered her pulse slow (60) without apparently giving it more strength.

Ordered :

℞ Unguent. hydrarg., ʒss.
Unguent. belladonnæ, ʒj.

S. Apply to left leg.

November 21.—Ointment did not help limb. Ordered following :

℞ Caffein. cit., gr. xxx.
Pot. acet., ʒij.
Syrup. aurant., ʒss.
Aq. ad., ʒij.

M. S. A teaspoonful every two hours in water.

November 23.—The last doses of mixture seemed to nauseate her. In fact she had one vomiting attack. Thinks it increased the amount of water she passed, although this was difficult to affirm, as she took yesterday acid drinks with about ʒij to Oj of cream of tartar, which moved her bowels freely. She does not have the same stimulating effects, in so far as her heart action is concerned as is given by fluid extract of convallaria. Breathing is certainly not as much relieved. True, convallaria does not benefit her dropsical symptoms notably, but it does not cause nausea or vomiting.

℞ Repet. convallaria gtt. v, every two hours. Hot air bath day after to-morrow.

November 25.—Breathes easily to-day, because, as she says, she has been sitting up in a chair all day; a considerable amount of watery, frothy sputa; took another hot-air bath to-day, with somewhat less fatigue than two days ago; appetite a little better; legs still very painful, although frictions with cocoa butter relieved their tension a little; pulse 72, fairly strong; heart sounds somewhat weak and muffled, and always very irregular and absolutely lacking in synchronism. Convallaria does not make her sleep any longer; was in a sort of half unconsciousness a great deal during the night; has been nauseated and vomited once every evening during last few evenings, after a severe paroxysm of cough. Does not attribute it, however, to convallaria. ℞ Repet. convallaria every three hours five drops, and every six hours 10 m. of tinct. ferri perchlor. with equal amount of spirits chloroform, glycerine and water every six hours. Continue vapor baths every other day.

December 3.—Have given her tinct. sylphium gummiferum, gtt. v., to be taken occasionally when troubled with difficulty of breathing. The sylphium appeared to give her some relief last night when attacked with great oppression and cough.

Hot air baths do not appear to give her sensible relief, and the fatigue of getting to and fro wearies her intensely. Her legs are very painful and swollen. She is seated nearly all the time in a chair. Her urine remains high-colored and small in quantity—not more than 16 ounces in 24 hours—for

several days past, and although she has been drinking freely of decoct. triticum repens. Stopped to-day mist. ferri, convallaria and trit. repens and ordered :

℞ Pot. iod., ʒj.
Caffein., ʒ iss.
Syr. aurant., ʒ iss.
Aquæ ad., ʒ iij.

M. S. ʒj every three hours, in half a wineglass of water.

December 4.—Showed great somnolence and complained of feeling dull and heavy in brain. Stopped mixture. ℞ Infusi digitalis ʒij every two hours.

December 5.—Had a bad night; could not sleep; to-day pulse irregular, depressible, about 72 per minute; heart action quite strong, less asystolie, more rythmic beats; mind clear; passed more urine, about one quart in last 24 hours; (must remark that she passed this quantity for the most part whilst taking caffeine with potas. iod. This mixture seemed to cause nausea and she began infusion digitalis this morning; when I saw her in the afternoon she had taken five doses. The lower limbs are less swollen, tense and painful. This benefit seems to be more due to caffeine and potas. iod. than to digitalis, since it was already marked before she began the use of the digitalis, which she only did because potas. iod. mixture nauseated her. Repet. infusion digitalis, ʒij. every two hours.

December 10.—Feels considerably better; passed nearly three quarts of urine in last 24 hours; legs diminished in size and less painful; abdomen also slightly diminished; has not slept well for some nights and last night took five grains Tully's powder, which gave her quiet rest of several hours; heart sounds stronger and more regular than they have been for a long while. Can now distinguish a murmur at first sound and at apex of heart, showing mitral regurgitation. P. 60. Infusion digitalis to be taken (ʒij) every four hours. Complains of pains and aches in different regions of body since swelling subsided. Takes very little food, and what she does swallow seems to distress her. Gave ʒj essence of pepsine after each meal.

December 17.—Very much better in every respect; legs are of normal size, abdomen much smaller, face less puffy, appetite improved, passes about three pints urine daily; pulse 60, stronger, but irregular; force of cardiac pulsations, as well as rhythm, much improved; asystolie only slightly marked; breathes decidedly better; no cough; has taken digitalis infusion ʒij during last two or three days every six hours and resumed small doses of mist. ferri perchlor. Repet. omnia.

PART II.

The lily of the valley, convallaria majalis, has been known many years to scientific observers, especially in its quality of a purgative plant, somewhat similar in its effects on the human economy to aloes, or scammony. As far back even as 1830, an analysis of its constituents was made by Valz, and two glucosides were separated from it and called by him convallamarin and

convallarin. Later on, in 1865,* Stanislas Martin discovered the alkaloid majaline. To this alkaloid and to convallamarin the special efficacy of the plant as a cardiac tonic is presumably due. This action, however, was but little dwelt upon by medical writers, and it was only after many attempts, that preparations have been made by pharmacists free of the purgative elements, notably contained in the resinous part of the plant. In 1867, W. Marmé† made a thorough study of the physiological action of convallamarin and convallarin on animals. These researches were published under the title of "Ueber Convallamarin, ein neues Herzgift." In dogs and cats poisoned by hypodermic injections of convallamarin (15 to 30 milligrams) the heart suddenly ceased to beat and this stoppage was preceded by clonic convulsions of mild type. He affirms that as a cardiac poison, it approximates in quality and quantity, digitaline and helleborine.‡ For many years convallaria has been employed in Russia as a popular remedy for dropsy. Few, or no detailed reports, however, as to its uses in this direction had appeared in medical periodicals until the year 1880. In that year there were published in the "Vratsch" some articles relative to the employment of this drug as a tonic of the circulation.§ Prof. Germain Sée, of Paris, became familiar with these articles and some other illustrative facts with respect to its use. So much impressed was he by the statements and the oral communication of Prof. Botkin, of St. Petersburg, that he determined to make a thorough trial of this drug. He made use of all the different pharmaceutical preparations and finally concluded that the aqueous extract of the flowers and twigs, (to which is added a third by weight of roots and leaves), of which the daily dose should be from 15 to 30 grs., was the most reliable and powerful of all. This extract has a bitter taste, is very soluble in water and alcohol and is of an agreeable, persistent odor. It may be given pleasantly in syrup in conjunction with an aromatic. A chemical analysis of convallaria made by Mr. Hardy, chemist of the Hotel Dieû, Paris, also, confirmed the statements already made known by Marmé, that the glucoside convallarin is extremely powerful in its action as a poison and resembles very much digitaline. A second glucoside, convallarin, contained in convallaria seems to be more or less inert in its properties. By numerous experiments upon cold-blooded animals, Sée discovered that a local application of a few drops of an aqueous extract of

*Union Pharmaceutique, quoted by Tanret.

†Nachrichten von der K. Gesellschaft der Wissens. Göttingen, 1867, p. 160-164. Bull. Gén. de Thérapeutique, 13, Août, 1882.

‡Marmé's conclusions are, also, reported in Schmidt's Jahrbücher, 1867, No. 5, p. 166, and in the New York Medical Journal vol. vi, p. 166-168.

§It is right to add here that a full report in regard to the action and uses of convallaria majalis was first given to American readers by Dr. Ralph d'Ary, of Romeo, Michigan, in the THERAPEUTIC GAZETTE, Oct., 1881, p. 392. Not only did Dr. d'Ary give his own experience, in the treatment of various forms of heart disease by convallaria, but he, also, furnished to the editors of the GAZETTE, translations of articles on this subject from the pens of Drs. Botkin, Troitsky and Bogojavlenski, of St. Petersburg. I regret to add that I was not familiar with Dr. d'Ary's work until it was too late to incorporate even a portion of it in my own article. B. R.

convallaria to the heart of a frog, will stop its pulsations immediately. In a less degree this holds true of the local application of this extract of convallaria to the hearts of animals higher in the scale. Convallaria was found to have no perceptible effect on the bulk of urine passed in twelve hours. It gave force to cardiac pulsations, rendered them slower, and established again a normal rhythm in cardiac action. The respirations were slower and deeper.

The action on the vagi was to dull their sensibility somewhat. If poisonous doses are given, the pulse becomes irregular and intermittent and finally the heart stops in systole, contrary to the effect of muscarine. Since Sée's experiments, the following conclusions have been reached by Ott in his investigations upon the physiological action of convallaria majalis:*

"1. That convallaria increases the arterial tension greatly at the same time as the heart begins to beat more frequently; that the heart begins to fail before the tension.

"2. The decrease of cardiac frequency is not due to cardio-inhibitory excitation, but to an action on the heart itself, probably its muscular structure.

"3. The rise of arterial tension is mainly due to stimulation of other vaso-motor apparatus than the main monarchical vaso-motor centre.

"4. The drug causes clonic spasms. If we compare the action of this drug with digitalis, it is found that the slowing of each is due to different causes; with digitalis it is due to cardio-inhibitory excitation; with convallaria some other part of the heart is the agent. Digitalis does not primarily accelerate the heart; convallaria does. After section of the spinal cord digitalis is powerless to increase arterial tension, whilst convallaria does. If now we compare the action of this drug with other cardiac agents, as aconite, urechites suberecta or astragalus mollissimus, it is found that it does not belong to this group. As aconite, urechites and astragalus resemble each other in their action, yet many important differences exist, so does convallaria differ from digitalis in several important particulars. The great rise of arterial tension would indicate its value in dropsies, reasoning upon Ludwig's theory of renal secretion. It is a drug which must not be pushed to any great extent, if I am to judge from a rather extensive experience with cardiac agents, upon the hearts of the lower animals."

In Prof. Sée's clinical cases we have twenty individuals treated with convallaria. Of these, all were affected with a notable degree of cardiac disorder, usually of chronic nature. In seventeen examples there was marked improvement. The most notable effects produced were those on the urine, the pulse, infiltration of tissue and dyspnœa. Within forty-eight hours after the exhibition of the extract of convallaria, the urine was notably increased in quantity and from one pint it frequently reached as much as six or seven pints in 24 hours. The pulse became slower, stronger, less unequal, and lost its irregularities. Little by little dyspnœa disappeared, so that after ten days, or two weeks, the patient was able to go up stairs without great oppression. In a similar manner the œdema and infiltration of the lower limbs gradually disappeared, the effusion into the abdominal cavity was con-

*Archives of Medicine, February, 1883.

siderably diminished. The breathing, also, became more profound and slower. The effects of convallaria upon the stomach have been rather favorable than the reverse. Far from causing inappetence, nausea, or vomiting, it was always borne with ease, and at times appeared to excite the appetite and facilitate the movements of the bowels. Incidentally, I should state here, that the experience of Sée in this regard, is opposed to that of Dr. A. H. Smith, who, in a case read before the Section on Practice, New York Academy of Medicine, Nov. 21, 1882, alluded to the fact of the stomachal intolerance caused by convallaria, and, judging by his own experience, was disposed to advise its employment by the hypodermic method in order to obviate this drawback. In many instances in which dropsical symptoms were accompanied by the usual attending dyspnoea, it was found that a combination of convallaria, with iodide of potash, acted rapidly and most efficiently.

Latterly, several contributions have appeared in regard to the use of convallaria majalis. Among these we should cite one in the *Paris Médicale*, March 25, 1882, p. 140; another by Dr. E. P. Hurd, of Newburyport, Mass., in the *Medical Record* of Sept. 9, 1882—and additional notes by the same physician in the *Record* of Nov. 11, 1882, and Feb. 17, 1883; another by Dr. A. H. Smith, in the *Archives of Medicine*, December, 1882; and still another very careful study by Henry Ling Taylor, in the *Medical Record* of January 27th and Feb. 3, 1883. Besides these, I would also refer to the remarkable case of vagus neurosis, with extremely rapid action of the heart, relieved by convallaria majalis, and reported to the Practitioners' Society of New York, at a stated meeting, Jan. 5, 1883, by Dr. Wm. M. Polk. In this case, as in one of Dr. A. H. Smith's cases, the convallaria was employed hypodermically, with excellent and rapid effects.

I should likewise mention the abstract of a paper which originally appeared in *Archiv. für Exper. Patholog. und Pharmacolog.*, Bd. xvi., s. 149, and which is given quite fully under the title of "On Digitalin," in the *London Medical Record*, Jan. 15, 1883, by Schmiedeberg.

This communication is a valuable critical digest of all that is up to the present time known regarding the action of digitalin and that of active principles akin to digitalin.

Amongst these, in class No. IV of Schmiedeberg, under the head "Amorphous Glucosides Very Soluble in Water, and Resembling Saponin," we find (15), Convallamarin, very like digitalin; from convallaria majalis.

Further, there is a short excerpt in the very last number of the *New York Medical Record*, Feb. 24, 1883, taken from the *Wiener Med. Wochenschr.*, Nov. 11th and 18, 1882, in which Dr. Berthold Stiller reports very indifferent success in the treatment of heart disease with convallaria. From his experiments, "Dr. Stiller concludes that convallaria, so far from being an efficient substitute for digitalis, is not worthy of even ranking as an adjuvant to this remedy in cardiac disease. He admits, however, that the specimens of convallaria used by him may have been of quality inferior to that employed by other observers who have reported such brilliant results." It is probable that Dr. Stiller may have been disappointed in his results on account of the par-

ticular kind of cardiac disorders he has been called upon to treat. It is not presumable that convallaria shall be equally valuable in all forms of heart disease. There must be, as for digitalis and belladonna, certain indications which should guide us in its use. Already one acute observer, Dr. E. L. Trideau,* of Saranac Lake, N. Y., after making use of the drug during one year in different cases, has come to the conclusion that convallaria is specially indicated and useful when the right heart needs stimulation as it frequently does, in cases of old mitral disease, and in those where chronic phthisis is present. In many examples of aortic disease, Dr. Trideau has found no benefit from the use of convallaria in relieving the symptoms which depended upon this affection. If I might be permitted to add a remark made to me in ordinary conversation, I would add that Dr. Francis Delafield is disposed to believe that convallaria will hereafter prove serviceable in cases of pneumonia, where there is appreciable failure in the contractile power of the right heart and in which digitalis is insufficient to give relief.

Now that I have given references to the observations and clinical experience of others, I shall refer to my own. I have given convallaria to four cases of asthma, in three of which, at least, there was evident chronic bronchitis and emphysema; in one case of enlargement of the heart, without valvular lesion, double pleurisy, with effusion and chronic Bright's disease; in one of sub-acute pericarditis, atheromatous degeneration of the coronary arteries and cystic degeneration of the kidneys; in one of chronic pericarditis, nutmeg liver and chronic diffuse nephritis; in one of combined mitral stenosis and aortic regurgitant disease; in four of simple dilatation of the heart, in one of which there was an intercurrent attack of sub-acute laryngitis; in two, marked cardiac irritability; in one of tendency to syncopal attacks; in one of cardiac hypertrophy and aortic stenosis; making in all fourteen cases. In eleven of them I have kept careful notes of the action of convallaria. In the other three cases, as well as in several which I have not mentioned, I have only the remembrance to guide me in what I am about to state. Before doing this, however, I shall read you the histories of eight of my cases.†

Case 1.‡—*Asthma Dependent upon Vesicular Emphysema, Relieved in a Remarkable Degree by the Internal Use of the Fluid Extract of the Root of Convallaria Majalis.*—The history was as follows: J. H., æt. 63, German, came to the out-door department of the New York Hospital, October 4, 1862. He complained of constant dyspnœa and sleepless nights. He was poorly nourished and his nose and lips were cyanosed. His health was tolerably good until 11 years ago, when he began to suffer from shortness of breath on exertion. At present, even the slight effort of putting on his shirt exhausts him. His mother and two of his brothers were affected in the same manner.

* N. Y. Med. Rec., March 3, 1883, p. 251.

†Three cases were treated after this paper was returned by the type-writer, and I could not incorporate them readily in the body of the article. One was a case of aortic stenosis, with hypertrophy, not benefited by convallaria; two were cases of cardiac dilatation and considerable irritability of heart action; both were relieved by the use of convallaria.

‡Case presented at a stated meeting of the Practitioners' Society, January 5, 1883 reported in New York Medical Record, February 3, 1883.

His voice is short and jerky, and he occasionally spits a small quantity of thick, gluey sputum, preceded by a cough of moderate intensity.

The expectoration of this substance relieves his dyspnœa somewhat for a time. His appetite is poor, his bowels obstinately constipated. He is compelled at night to assume a semi-recumbent posture in order to obtain any sleep at all.

Physical examination of the lungs reveals great emaciation of the chest walls; shoulders high; back much bent over; thorax dilated at the base; sterno-mastoid, scaleni and trapezius muscles are prominent during inspiration; chest moves as a whole in a vertical direction during the respiratory acts; third and lower intercostal spaces are sucked in visibly with each effort to breathe. Alæ of nose are markedly distended; expiration is stertorous. Superficial veins of arms and forearms are much dilated. There is considerable pulsation of the brachial arteries at the elbows. On percussion hyper-resonance covering a wide area is discovered, which is especially pronounced on the left side of the thorax. Auscultation anteriorly gives rough inspiration with numerous sonorous rhonchi on both sides; expiratory sounds are feeble. Posteriorly, inspiratory vesicular murmur is very feeble; expiratory sounds are loud, and accompanied with disseminated dry râles.

Physical examination of the heart shows apex beat in fifth intercostal space to left nipple; epigastric pulsation diffused; cardiac beats are but feebly felt; atheromatous changes in arteries are at an advanced stage. There is a faint blowing murmur synchronous with the systole, and heard with greatest intensity outside and somewhat below the left nipple.

Patient's symptoms always become more accentuated toward evening. Atmospheric changes have no obvious influence upon their character or degree. Country air in past time has apparently given him relief from his continued oppression. Several years ago, while in Rockland county, he felt much better than usual. At present he is prevented from leaving the city on account of his narrow means. Latterly he has taken medicine sparingly; in former years he took large quantities of different kinds of medicine. Spirit of camphor, in 20 gtt. doses, formerly gave him great temporary relief. He is now very much annoyed by a condition of cutaneous irritation, which has occasioned prurigo to an excessive degree.

October 4, 1882.—At 3:50 P. M. fluid extract convallaria, Mxv, were given by the mouth. Twenty minutes later patient states that he breathes with much greater ease, notwithstanding a rapid walk of several minutes' duration through the waiting-room of the hospital.

℞ Fl. ext. convallariæ, Mjv
Syrupi tolutani, Mviiij
Aquæ, q. s., ad., 3j.

M. S. To be taken by the mouth every three hours.
October —

℞ Fl. ext. convallariæ, gtt. v.

S. Take every three hours.

October 16.—Medicine seems to benefit him, inasmuch as he continues to breathe with greater comfort to himself.

October 20.—*Statu quo*—continue treatment.

October 27.—Repeat treatment.

November 8.—Repeat treatment.

Patient states when dyspnœa becomes more intense, as it sometimes does, in a paroxysmal manner, he increases the usual dose by several drops.

November 20.—Repeat recipe.

December 1.—Increase dose of convallaria to gtt. x every three hours.

When patient is at home and in repose, his breathing is much freer than formerly. While taking moderate exercise it is still very short and shallow, but if he rests for a short time afterward his respiration again becomes relatively quiet, and is decidedly improved over what it was under like circumstances, before he began to take convallaria.

December 22.—Patient rests quietly at night. He can sleep now lying down, but is as yet unable to work on account of debility. His appetite is poor.

During the past 17 years he has taken a great many drugs, prescribed by various physicians, but affirms positively that he never got much relief from any medicine until the present time. Since convallaria was first taken his breathing has continued steadily to improve. The quantity of urine passed has always been abundant, and has not appreciably increased under the new treatment. Repeat medicine.

December 29.—Feels about the same. Amount of urine passed in 24 hours measures one quart. Estimation was made on two occasions. Recipe as above.

Formerly, when able to work, the man had been employed in a sugar factory, and afterwards in a tobacco factory.

Case 2.—**Chronic Bright's Disease—Dilatation of the Heart—Pericarditis.*—The following history was written for me by Dr. Charles Beach, junior assistant on the medical division of St. Luke's Hospital :

H. G. had had numerous rheumatic attacks, involving one or both ankles. The last attack occurred eight months ago, when the knees were involved. It lasted six weeks. She had never had any cardiac symptoms. In July, 1882, she was exposed to cold and damp air, since which time she has been failing in strength. Micturition had been frequent, spots floated before her eyes, and she had suffered from nausea. Two months ago she began to have dyspnœa, somewhat paroxysmal in character, and œdema of the feet, legs, hands and face appeared. At various times she had had moderate pain in the left side of the chest. On admission the patient had marked œdema of the face and extremities, was suffering from extreme dyspnœa, had a very weak pulse, no appetite, and her temperature was elevated. Digitalin and whisky were administered hypodermically. The urine had a specific gravity of 1010, acid reaction, contained fifteen per-cent. of albumen, but the micros-

*Specimens were presented at a stated meeting of the New York Pathological Society, Dec. 13, 1882. (See New York Medical Record, Jan. 13, 1883).

copical examination was negative. Both pleural cavities were about half filled with fluid. Examination of the heart was negative. Thirteen ounces of fluid were withdrawn from the right side of the chest. Immediate and marked relief followed :

Physical Examination : Respiration 32; pulse 108 and tense; the apex beat could not be felt. Pericardial friction-sounds were heard midway between the apex and the left border of the sternum. The first sound of the heart was prolonged. There was evidence of pericardial effusion, and also of fluid in the left pleural cavity. The spleen was slightly enlarged. The dyspnoea was believed to be chiefly uræmic. A milk diet was ordered. Half an ounce of whisky was administered every six hours. One minim of a one-per-cent. solution of nitro-glycerine was ordered every four hours.

October 27.—The patient had a chill this morning lasting fifteen minutes; also vomiting. During the last twenty-four hours she has passed sixteen ounces of urine. The nitro-glycerin was reduced to one drop three times a day. The vomiting persists. The bowels were moved by enemata. Cups were applied to the loins.

November 1.—Physical examination revealed dullness up to the angle of the scapula. Nitro-glycerin was discontinued. Over the apex of the heart there could be heard, on inspiration and expiration, a rubbing sound, not affected by the heart motion, but still believed to be probably pericardial. The urine had a specific gravity of 1.008 neutral reaction, and contained thirty per cent. of albumen. The patient had passed twenty-four ounces during the past twenty-four hours.

On November 2 the cardiac sounds were distant and indistinct; crumpling sounds were still heard. Cardiac dilatation, localized pericarditis. Whisky was continued three times a day. The fluid extract of convallaria, ten minims, were administered every six hours. From November 4th to November 9th the patient received whisky and the fluid extract of convallaria and the quantity of urine passed varied from twelve to twenty-two ounces in the twenty-four hours. On that date pericardial friction-sounds were noticed preceding the second sound of the heart. Pulse 96.

On November 11th the right side of the chest was aspirated and thirty-five ounces of fluid were withdrawn.

On November 12 the patient passed ten ounces of urine which had a specific gravity of 1.014, was alkaline, and contained sixty per cent. of albumen. On November 15 the œdema of the feet and legs had increased. On November 16 there was œdema of the vulva. Patient passed fourteen ounces of urine. A creaking sound was heard over the pericardium. November 18 the pericardial friction-sound had almost entirely disappeared. The patient's pulse was 72 and regular; she passed twelve ounces of urine. The convallaria and the iodide of ammonium, which had been administered since November 8, in doses of two grains, were then discontinued. On November 19 the hot air bath was administered. On November 20 the patient passed only eight ounces of urine, and had pain in the back and lumbar region. From this date to November 22 there was no marked change in the condition of the patient and on the 24th she died.

At the autopsy the abdominal walls were found infiltrated with serum, and the abdominal cavity contained about eight ounces of fluid. There were about ninety-eight ounces of serous fluid in the pleural cavities. There was about one ounce of serum in the pericardium, over the apex of the heart anteriorly. Just to the left of the septum was a small patch, about the size of a split pea, of thickened plastic exudation. On the posterior surface of the aorta, just above the reflexion of the pericardium, were seen patches presenting the same appearance. The right ventricle was distended and contained dark and white clots. The left ventricle was hypertrophied. The valves were apparently normal. The heart weighed fifteen and a half ounces. The lungs were more or less compressed and the pleura was thickened. The spleen was enlarged and the capsule thickened; weight nine ounces. The capsule of the liver was thickened, especially about the inferior ligament, and the surface showed white streaks with some increase of connective tissue. The kidneys were the seat of chronic intestinal nephritis. Both were reduced in size, the left weighing only an ounce and a half. There were cysts in both ovaries.

Attention in this case is directed to the use of convallaria and nitro-glycerin. Both these remedies were employed and there was no noticeable increase in the quantity of urine passed. Evidently under the influence of convallaria the cardiac action was increased in force and the heart was made to do its utmost, and apparently the woman would have been benefited except for the condition of the kidneys. While the patient was taking the iodide of ammonium a pericardial friction-sound disappeared, and at the autopsy it was believed that the evidence of disappearing pericarditis was found.

I believe in those cases where we find a low specific gravity of the urine, and its quantity cannot be increased by the best known cardiac stimulants, that the atrophic kidney usually exists, and we should all be prepared to assume that with a small quantity of urine with nothing specially abnormal about the specific gravity, and failure on the part of the kidneys to respond to cardiac stimulants, as in the case recited, there is at least a reasonable probability of finding that form of kidney degeneration.

Case 3.—*The following history was furnished me by Dr. R. J. Devlin, senior assistant to the medical division of St. Luke's Hospital: The patient was 44 years of age, entered the hospital December 1, 1882, and was able to give only an imperfect history. His first and only attack of rheumatism occurred seven years ago, which involved the ankles and hands, and lasted, including relapses, four months. He had never suffered any pain or distress in the region of the heart, nor palpitation. During the last two years he had been obliged to rise from four to six times during the night to pass water. No change had been noticed in the appearance of the urine. The patient thinks that the daily quantity has been excessive. During the last six months he has suffered considerably from sweating and diarrhœa. Last August he was seized with sudden failure of vision in the left eye, followed in about

*The heart and kidneys of the patient whose case is here reported were presented at a stated meeting of the Pathological Society, Dec. 13, 1882. (See New York Medical Record, an. 13, 1883).

two months by similar changes in the right eye, and at the time of his admission his vision was not sufficiently good to enable him to read print. Œdema of the extremities appeared for the first time two months ago.

On December 2d, the abdomen being very tense, he was tapped, and 20 ounces of fluid were removed.

From this date to December 8th, there was a gradual decline of the patient, pericardial friction-sounds and valvular murmurs were distinctly heard, the œdema increased, there was no increase in the flow of urine, the patient became delirious, finally comatose, and died. At the autopsy there were found some thickenings of the cardiac valves, with atheromatous degeneration of the anterior coronary artery, and the kidneys were the seat of cystic degeneration. Patient was treated with caffeine, iodide of ammonium and infusion of digitalis.

Case 4.—*Mitral and Aortic Valvulitis; Cardiac Enlargement*.—I. K., 32 years of age, married, German, stone-cutter, was admitted to St. Luke's hospital, December 15, 1882. Patient has had four attacks of acute articular rheumatism. The first attack was in 1864; the last in 1880. He denies cardiac symptoms until six weeks ago, when he began to have slight œdema about the ankles and frequent micturition. Two weeks ago œdema became considerable and patient began to suffer from severe dyspnœa. On admission, the infiltration of the lower limbs was well marked, and there was a moderate amount of fluid in the abdominal cavity. The phalanges had the familiar drum-stick extremities and the difficulty of breathing was extreme.

Examination of urine gave specific gravity 1.012; acid; albumen 25 per cent.; under microscope, blood disks, renal cells, hyaline and granular casts.

℞ Milk diet.

℞ Fl. ext. convallariæ, M x, q. three hours.

December 16.—Physical examination showed apex beat one inch outside left nipple in the sixth intercostal space. Heart considerably dilated; marked apex thrill; intense dyspnœa; murmurs at tricuspid and mitral orifices synchronous with systole. Judging from pulse, it was also probable that regurgitation existed at the aortic orifice.

December 17.—Passed 36 ounces of urine in last 24 hours.

December 18.—Aortic regurgitant murmur now more marked than that at the mitral orifice; a few sub-crepitant râles during respiration on both sides of the chest posteriorly, pleuritic in character. Passed 40 ounces of urine yesterday.

December 19.—Urine fallen to 26 ounces. Increase convallaria to gtt. x, q. two hours; considerable dyspnœa remains, but less than previously. Difficulty of breathing both in inspiration and expiration; no nausea; pulse stronger.

December 20.—Moderate epistaxis during the night; urine fallen to 20 ounces; no improvement of urinary secretion from the use of convallaria—stop it.

℞ Infusion digitalis, 3 j, t. i. d.

December 21.—Breathing easier; did not sleep well; increase digitalis to 3 j q. four hours.

December 22.—Pulse 72, regular.

December 23—P. M.—Erysipelas distinguished on forehead.

December 25.—Erysipelas over face.

R Brandy, ʒss, every four hours.

Tr. chloride of iron, gtt. xxv, t. i. d.

December 26.—Erysipelas spread over cheeks; tr. of iron stopped. During last 24 hours urine rose to 50 ounces. Patient transferred to isolating ward.

R Milk and lime water; lead and opium externally.

December 27.—Stimulants increased; erysipelas stationary.

December 28.—Facial aspect improved; quantity of urine diminished, but precise quantity passed not noted.

December 30.—Erysipelas subsided; difficulty of breathing intense; amount of urine 13 ounces. Patient began breathing noisily, almost stertorous at times.

December 31.—At 5:45 A. M. patient died suddenly on night chair; day previous was feeling better up to 6 P. M., and suffered less from dyspnœa.

Note.—Urine in this case was not increased by digitalis, or convallaria, but was much augmented by the use of tr. chloride of iron. Patient complained after taking the iron of feeling much weaker and of increased difficulty in breathing, although the urinary secretion was more active.

Autopsy.—Right pleural cavity half full of clear fluid; left cavity contained 7 to 8 ounces, of similar fluid; slight amount of serous fluid in the pericardial sac; new adhesions of plastic lymph over the left auricle and left ventricle; also adhesions and deposits over right heart; weight 22½ ounces; aortic valves atheromatous, and bound down in part; contained vegetations; mitral valve markedly calcareous in places, contained large bony masses as large as sharpened end of lead pencil; free borders thickened, causing stenosis and regurgitant condition. Tricuspid valve normal; left lung had some adhesions at apex; right lung had recent adhesions at apex. Left kidney large, pale, cortex thickened; weight 5 ozs.; right kidney similar changes; weight 4½ ozs. Both kidneys show distinct parenchymatous degeneration. No fluid in abdomen.

Case 5.—*Cardiac Dilatation.*—The case was that of a woman 42 years of age, widow, born in the United States, seamstress, who entered St. Luke's Hospital December 21, 1882, with the following history :

Patient never had rheumatism. Eight years ago had general anasarca; has suffered from palpitations one year, swelling of hands and legs more or less, during that time; no headache; morning nausea several months; six months ago œdema of feet increased; scanty urine one year; cardiac palpitations worse latterly; vision normal; dyspnœa for some time past on slight exertion; patient is just at menopause and complains of nervousness; appetite poor; bowels relaxed; marked œdema of legs; examination of urine shows specific gravity 1012, neutral, trace of albumen; microscopic examination negative.

December 22.—Pulse compressible and dicrotic but otherwise regular; no abnormal murmur in præcordial region; normal heart sounds feeble and distant; slight epigastric pulsations.

Diagnosis.—Simple dilatation of the cardiac cavities:

R Fl. ext. convallariæ, gtt. x, q. 3 h.

Patient passed 24 ounces urine daily.

December 24.—Patient passed 24 ounces urine during last 24 hours.

December 25.—Edema of legs has subsided; no dyspnœa.

December 27th.—Slight systolic murmur in third intercostal space, possibly due to anæmia. Pulse apparently stronger.

December 28.—Still passing about 24 ounces of urine daily.

Note.—Convallaria has completely relieved palpitations, but has not increased the quantity of urine passed in a given time.

Case 6.—A young girl suffering with a sub-acute attack of catarrhal laryngitis already of several days' duration.

The cervical ganglia on the left side of the neck were painful and engorged; the voice was hoarse, there was moderate soreness, or pain in the throat and there was slight cough. The cardiac pulse depressible. On palpation the apex beat could not be discovered and by percussion the heart was shown to be dilated. Convallaria was given every three hours in doses of 5 gtts. in mixture, with a view to stimulate heart action and in this way to lessen the congestion of the laryngeal mucous membrane. In 24 hours the hoarseness and cough had both diminished, and the heart beats and pulse were slightly increased in force. Afterwards stimulating inhalations were used, the convallaria was continued and the patient soon was convalescent. The effects on the kidneys were not remarked.

Case 7.—*Chronic Pericarditis; Nutmeg Liver; Diffuse Nephritis.*—Chas. M. Good, æt. 40, S., Eng., musician.

December 15, 1882.—Was admitted into St. Luke's Hospital.

Patient had an attack of rheumatism 17 years ago, and another 9 years ago, each involving all the large joints. The present attack began last April, and, with periods of exacerbation and remission, has lasted up to the present time. All the joints have been affected at one time or another. The hands and wrists have been most severely involved. There has been pain and stiffness but little redness and swelling. Has noticed præcordial pain and also palpitation since beginning of last attack. Also subject to attacks of vertigo. Appetite good. Bowels regular. Pulse and temperature normal.

Examination of urine 1.010; neutral; regular.

December 16.—Patient has severe pain in both wrists and ankles; no redness; no swelling; some heat. Slight pain in knees. Examined by H. P.

Mitral systolic murmur heard at apex and at base transmitted into axilla.

R Potas. iodid., gr. x, t. i. d.

December 18.—Increase iodide to gr. xv, t. i. d.

Examined by Att. P.: Regurgitation at both mitral and aortic orifices. Aortic bruit increases downward and to left. L. aortic cusp. chiefly affected.

December 20.—Patches of erythema all over body. Stop potas. iod.

December 28.—

℞ Potas. iod., gr. x, t. i. d.

January 7, 1883.—Patient does not bear iodide well—stop it.

January 9.—Pain in shoulders.

℞ Mist. acid salicyl., ℥ ss, t. i. d.,

January 11.—Marked improvement under use of mist. salicyl.

January 13.—Pain very much improved, but not entirely controlled. Stop mist. salicyl.

℞ Tr. ferri chlor., M xxv, t. i. d.

January 15.—Pains have returned while on tr. ferri chlor. Stop tr. ferri chlor.

℞ Mist. salicyl., 3 ii, s. q. Two hours.

January 16.—Much less pain since yesterday.

January 17.—Evening : Reduce mist. salicyl. to q. Six hours.

January 20.—Patient complains that medicine causes headache. Stop mixture. salicyl.

January 21.—Pain increasing; also complains of soreness over pericardium,

January 23.—Had some pulmonary œdema last night. Heart rapid and weak. Ordered cups and mustard. Same condition exists to-day, though to a less extent.

Examined by Att. P.: Doubling of first sound at apex. No murmur. Rythmical irregularity of pulse. Sub. crep. râles over lower half of both lungs. Breath sounds slightly more feeble at right base. No pericardial effusion. Pulse 160. Hypodermic of ext. convallaria fl., M viii, administered over heart; no benefit derived. Repeated in half hour, and pulse reduced to 80 within hour-and-a-half after second dose. Last night patient was ordered ext. convallaria fl., Mix, s. q., four hours, and brandy, ℥ ss q., four hours. To-day : Morph. sulph., gr. i-12, s. q., four hours.

℞ Tr. belladonnæ, M v, s. q. Four hours.

January 23, P. M.—Morphia stopped.

January 24.—Pulse 108; more regular; no dyspnœa. Patient quite comfortable; sweating profusely.

Examined by Att. P.: Pulse 108. Regurgitant bruit heard distinctly after second sound.

January 25.—Stop convallaria and belladonna.

℞ Digitaline, gr. i-100 t. i. d. by mouth.

January 26.—Increase digitaline to gr. i-50 t. i. d. Pulse 100; regular. Hydrocele of 1. cord.

January 27.—℞ Light diet.

Examined by Att. P.: Pulse again rapid and uneven. Possibly ulcerative endocarditis.

P. M.—Temperature 103 deg. Stop digitaline.

℞ Infus. digitalis, 3 i, q. i. h.

January 28.—Pulse 102. Reduce digitalis to 3 i q., two hours.

January 29.—Pulse 100. Some præcordial pain.

Examined by Att. P.: Murmurs again distinctly heard. Mitral systolic and aortic diastolic. Doubling of first sound marked at xyphoid cartilage.

January 30.—Pulse 94.

January 31.—Pulse 84-90; very irregular and intermittent, but full of strength.

Examined by Att. P.: Reduce digitalis to 3 i q., three hours. Doubling of first sound, but no murmur; valves not calcareous. Probably heart is dilated, but the muscular tone about orifices is well preserved.

February 1.—Dr. Kinnicutt's service.

Examined by Dr. Kinnicutt: Apex, 6 sp. line of nipple.

February 2.—Several loose movements, very offensive in character, accompanied by a good deal of pain. Heart active; more regular. Aortic direct murmur less loud.

February 3.—Bowels costive; painful defecation. Movements very offensive.

℞ Ol. ricini, 3 ii.

Examined by Att. P.: Over aortic area, a distinct systolic murmur transmitted up and down sternum and along costal cartilages. Less intensity over pulmonary area. Distinct diastolic murmur heard along sternum from second interspace downward. Hypertrophy in excess of dilatation. Marked heaving impulse. No increase in liver or splenic dullness.

February 4.—Reduce infusion digitalis to 3 ss.

February 5.—Præcordial pain again marked. Blister ordered over præcordium.

February 6.—Reduce digitalis to 3 ss q., four hours.

February 7.—Diarrhœa still troublesome.

℞ Ac. carbol, M-4

Tr. opii, deod., Mij. M. s. q., three hours.

February 8.—Ex. urine 1028; ac. large amount ovates.

February 9.—Has three murmurs. ℞ Morph., gr. 1-12, q. four hours—stop ac. carbol, and tr. opii.

℞ Hydrarg. bichlor., gr. 1-20, q. three hours.

February 10.—Stop digitalis. Increase morph. to q. three hours.

February 15.—Pulse has continued pretty regular and of good volume. During the past two days a marked fusiform dilatation has apparently formed on R Common costal cartilage, which pulsates violently. Examined by Att. P.: Heart acting well, but respiration becoming very irregular. P. M.—Patient comatose; extremities cold; pulse very full. 10:30 P. M. patient died.

AUTOPSY.

February 16, 1883, at 3:00 P. M.—Body fairly nourished; rigor mortis fairly marked; œdema of legs; knee joints swollen, right more than left.

Peritoneum.—Small amount of fluid; no evidence of peritonitis. Diaphragm fourth rib right; fourth space left.

Thorax.—Heart almost entirely uncovered by lung; adhesions generally distributed over right side; a few adhesions on left; right pleura contains $\frac{3}{4}$ viij of yellowish serum.

Pericardium.—Two layers firmly adherent by old adhesions.

Heart.—Enormously increased in size; left ventricular wall hypertrophied; left ventricle very greatly dilated; right ventricle moderately dilated; tricuspid valve thickened along free border; pulmonary valve normal; aortic valve has its cusps thickened, especially along the free border; the segments are retracted; there are vegetations along free border; segments of mitral markedly thickened with slight vegetations on free border; muscular tissue very fatty; aorta atheromatous.

Lungs.—Left lung badly acrated, congested and very œdematous; bronchial tubes congested and covered with mucus; right lung ditto.

Spleen.—About normal in size; quite hard local thickenings of capsule.

Kidneys.—Left slightly increased in size; capsule adherent in places; surface granular; tubes both of pyramids and cortex show fat; markings fairly well preserved in places; chr. diffuse nephritis.

Stomach.—Mucous membrane congested and thickened.

Bile Duct.—Previous.

Intestines.—Small intestines congested in places; hemorrhages beneath mucous membrane of descending colon.

Gall Bladder.—Filled with dark bile.

Liver.—Nutmeg; small; central vessels dilated; congestion of portal vessels; small amount of fat; small amount of fat at periphery of lobules; connective tissues around portal vessels increased.

MICROSCOPIC EXAMINATION.

Heart.—The cells of the heart are everywhere very fatty; the transverse striæ are wanting, almost entirely.

Liver.—The central vessels are dilated, and the peripheries of the acini are anæmic and fatty; there is bile pigment in the hepatic cells, surrounding the central vessels; there is intense congestion of the intra lobular plexus and atrophy of cells in their neighborhood.

Kidneys.—The connective tissue is increased in places; there is extensive fatty degeneration of the epithelium lining, both the straight and convoluted tubules.

Case 8.—*Tendency to Syncopal Attacks Relieved by Convallaria Majalis*.—A young lady, 22 years of age, single, residing in one of the healthiest situations of New York, came under my care about two years ago for chronic rhinitis. She was pale, anæmic, with considerable local pain over lumbar and lower abdominal region at the time of her menstrual flow. There was no history of

constitutional dyscrasia of any kind. Her father and mother and several sisters have always had good health. Her nasal trouble has not improved much, notwithstanding assiduous treatment of the most approved kind, both local and general. Her nutrition, also, appears to remain in about the same imperfect state. During the past two or three months she has been treated by me for obstinate atonic dyspepsia for which her family medical adviser formerly treated her with only moderate success. This winter her dyspepsia has annoyed her as much as previously and accompanying it she has suffered from frequent faint turns. These faint feelings, during which her hands would become icy cold, her pulse almost disappear at the wrist and her face be overspread with deathly pallor, lasted an hour or more. She has been taken suddenly with these attacks in church, at the theatre, in the street, in her own home, sitting, or standing, or even when quietly reposing in bed. At first I examined her urine very carefully and found it, on repeated occasions, in a healthy condition. The heart action was weak, but regular and with no abnormal murmurs. I concluded that the attacks were caused by the condition of the stomach and used many usual remedies to relieve the dyspeptic condition, which I finally succeeded in improving to a marked degree. The faint turns continued as before. I now examined her ears, found impacted cerumen, removed it, and after using Politzer's bag, found by the ordinary tests that her hearing was very good. I now gave five-minim doses of fluid extract convallaria every six hours with a view to stimulating cardiac contractility and thus cure the faint turns. When seen one week after the use of the remedy I found my patient decidedly improved. She had had only one faint turn in the time since my previous visit, although prior to taking convallaria she had an attack resembling syncope almost every day. Her dyspeptic condition was notably improved, and, in fact, she felt altogether better in health, and when I suggested giving up the use of convallaria she objected to it in no uncertain tones.

Upon auscultation of the heart on this occasion I found evident reduplication of the first sound of the heart heard over the entire præcordial area. The heart beats were somewhat more forcible than at a previous examination, but not apparently so much benefited as regards their power, as I should have presumed would be true in considering her much more comfortable condition.

It will be remarked as regards the influence of convallaria on

1.—*Digestive Organs*.—On two occasions I have seen decided nausea and even vomiting follow closely upon the exhibition of the fluid extract of convallaria. Inasmuch as at the time the patient was passing a relatively small quantity of urine of low specific gravity, which contained from 5 to 15 per cent. of albumen, I was not convinced that the convallaria was responsible for the stomachal intolerance, but thought it could be with equal propriety attributed to commencing uræmia, or indeed to simple chronic congestion of the gastric mucous membrane under the dependence of weakened heart power.

2.—*Heart, Pulse, Respiration*.—Whenever the cardiac beats have been

very irregular, unequal, or intermittent, I have not seen these conditions much changed even by the exhibition of quite large doses (10 gtt. every three hours) of convallaria continued for several days at a time. At best all I have remarked after a few days was somewhat greater force of each successive cardiac contraction. I have given it to two patients with acute painful palpitations with the greatest benefit (case 5).^{*} The number of the cardiac beats has been lessened a few beats on several occasions; thus the pulse has fallen from 108 to 96 per minute; but I have only remarked once a rapid and considerable diminution in the cardiac acceleration, (case 7), and this was occasioned, not by giving the drug by the mouth, but by means of hypodermic injection. The case was one of chronic cardiac disorder in which the pulse was beating at the rate of 160 per minute. It was reduced in one hour and a half and by two hypodermic injections, at one-half hour interval, to 80 per minute and with evident relief to the patient. On one occasion it was noted that after each dose of convallaria the patient had a strong desire to sleep (case 4, p. 7) and in fact did sleep for an hour, or more, awaking from it with a decided restful feeling and much quieted by the long needed repose. Whether, however, the convallaria produced this happy result by a direct effect upon the intra-cranial arteries, or whether it lessened those throbbing sensations which, in nervous patients affected with chronic heart disorders, are so apt to cause sleeplessness, I did not at the time determine, and must wait for further opportunities to satisfy myself on this point. It has seemed to me by palpations of the pulse of the patients who were taking frequent doses of convallaria that the pulse beats showed decidedly increased vascular tension. Still no sphygmographic tracings were taken to determine this point with great accuracy. What I can affirm, however, is that while giving convallaria I have never noted any symptoms showing sudden cardiac depression, or failure in its contractile force, such effects, indeed, as have been remarked in experiments upon animals with this drug. There does not appear, therefore, within reasonable limits of doses, to be any risk of producing poisonous effects by its employment. In this respect it has an evident advantage over digitalis, which, as we know, will finish by wearing out heart action and increasing at times the rapidity of the cardiac beats rather than diminishing their number, the effect which we especially wish to accomplish. The cumulative effects, in a word, of convallaria, are not to be feared in man as those of digitalis, and this fact we explain by its rapid elimination from the economy, and probably by the fact that convallaria acts more particularly as a stimulant of the peripheral fibres of the vagi than as an agent which affects directly the cardiac muscular fibre.

3.—*Respiration*.—Convallaria has occasioned more freedom of the respiration—the patients have manifested less anxiety and oppression on account of difficult breathing—than before its exhibition. This it has accomplished in rendering the inspirations slower and more profound.† On one occasion,

^{*}The other case was one of cardiac dilatation referred to in foot note p. 14.

† This clinical observation does not correspond with that of Smith, in his first case, who says, "that convallaria quickens the breathing;" nor, indeed, with the physiological experiments of Marmé. Ott does not give his conclusions in regard to the respiration.

where I combined the use of convallaria with that of iodide of potassium, I did not see any additional good effect on the ease of breathing caused by the mixture of the two drugs. On the other hand, I was soon obliged to give up this treatment on account of the obvious nausea and vomiting thus occasioned.*

4.—*Diuretic Effects.*—As regards these, I must here separate myself very categorically from the observers who have preceded me. Instead of finding in convallaria the valuable renal stimulant which I had reason to expect from my reading, I found the urine was scarcely or at all increased by its exhibition. Further, no sensible change in the appearance, specific gravity, or composition of the urine, was noted in the patients submitted to this treatment. The œdema of the lower extremities, the serous effusions into the different cavities of the body, of the peritoneum, the pleura, and within the pericardial sac, did not disappear, or even notably diminish whilst it was given. In one remarkable case (Case iv, p. 268), in fact, in which it had been used without the slightest notable good effect in this regard. Infusion of digitalis was then given in ʒij doses every two hours, and within three or four days' time, very considerable effusions into the different large cavities of the body had greatly diminished, and the lower limbs, hands and face, instead of being swollen and tense, or merely puffy and softly œdematous, became almost of natural appearance. The urine, meanwhile, from the pint in the twenty-four hours, had increased in quantity to three quarts, and the patient was, as it were, resurrected, so remarkable was the improvement of almost all distressing symptoms. It is just possible that the fact of an evident advanced state of renal degeneration will explain why convallaria failed to increase the urinary secretion in two or more instances where it notably failed to produce any appreciable good results. But this explanation will not suffice for the last case referred to (Case iv, p. 7), since in that instance no albumen was ever present in the urine, nor any deposit which could in any way reveal kidney degeneration of chronic nature. The renal complication, if there were such, could have been nothing more than the chronic congestive condition which so frequently accompanies chronic cardiac disease.

5.—No symptom of poisoning, nor any direct effect upon the central nervous system, has been remarked by me in my use hitherto of convallaria,†

In concluding this paper, I would suggest a question for solution of very great importance and which, so far as I know, has never been presented before by any writer, except Huchard: Are there not several kinds of asystolie, as there are various remedies which act as tonics of the heart?

Evidently digitalis, convallaria, caffeine, nitro-glycerine, have some points

* This combination was tried on account of the statement of Sée, that in cases in which great dyspnœa was present, it would be found useful.

† The preparation given by me was the fluid extract of the root manufactured by Parke, Davis & Co. The doses were usually 5 to 10 gttis. every two, three or four hours in some agreeable menstruum. Once or twice I believe the fl. ext. of the flowers was given. As I am informed, the home-made supply of this latter preparation is for the while almost exhausted. (V. also note of Dr. Hurd in Med. Rec.) It is lighter in color than the fluid extract of the root.

of similarity in their manner of influencing heart power and heart structure, but it is, also, apparent, even after my own imperfect study and comparison of their effects, that they differ considerably. In what these differences consist is at present only known in part, and it will require future study and observation to limit their indications more accurately. Sufficient is already determined, however, to enable me to affirm positively, that as we possess several medicinal agents which have each its special tonic influence over the heart, so we have cases of asystolie which are occasioned in different ways, although ultimately giving many physical and rational evidences of a strong likeness between them. Unfortunately, it is not as yet in the power of the most accurate clinical observer to say when one structural cardiac constituent is affected morbidly, and when another. Moreover, it should not be lost sight of that whilst in the first stages of organic heart disease it may be practicable to discover the inter-dependence of the lesions, and to recognize the starting point of the morbid processes, yet in the more advanced period it shall scarcely become possible. When nerves and ganglia, vessels and muscular fibre are all degenerated, it would be almost folly to affirm that in this or that change of elementary structure we had found the cause of the symptoms presented. But before the final stage and during a long period when cardiac rhythm is much affected, when the pulse is unequal, irregular and intermittent, when the urinary secretion is deficient, and general anasarca, more or less developed, with dyspnoea of variable amount prevails, we may hope that distinguishing features may yet be described which will permit of accurate differential diagnosis. I am personally convinced, even at this time, that some cases of asystolie hitherto considered as due to fatty degeneration of the cardiac walls are mainly the result of incoördinate or insufficient action on the part of one or more of the nerve structures governing the heart. It may be the vagi, the sympathetic, the cardiac ganglia, which are implicated specially, and as one or other is primarily diseased, so our cardiac symptoms and signs may differ in a measure; only in what this difference consists precisely, we have not hitherto discovered. Again, the entire action of a heart affected with "asystolie" may be controlled by vascular changes, and if we knew how and when to recognize this fact, we should have good reason for giving a therapeutic agent distinct from the one employed for other affections of an analogous though, in reality, separate kind. Some one may urge in reply to this statement that it is hardly possible to be deceived as to the efficient causes of symptoms presented during life, when at the autopsy one finds dilated heart cavities and fatty degeneration of the muscular fibres. I reply that, of course, such instances are frequent, and were it not that in them I recognize a final stage of several different primary changes, I should find it impossible to offer a solution. But let it be remembered that, at times, cardiac cavities are only moderately dilated, without the slightest accompanying fatty change of the muscular fibres, and yet previous to death we have had many familiar signs of asystolie. The autopsy, if carefully made, may or may not afford us a plausible explanation of a curious fact. I feel assured, however, of one thing, viz., that only when pathological researches shall have revealed in all doubt-

ful cases, the intimate morbid alterations of the nerve trunks and ganglia, controlling cardiac action, shall we be able to affirm that there is or is not an actual lesion to explain the symptoms during life. Even if anatomical investigation should ultimately prove insufficient, there may still be some work in the direction of pathological chemistry, especially in the analysis of the solids or fluids of the economy, through which obscure matters will gradually become lucid. In order to show that something already has been acquired to our knowledge of facts pertaining to the elective action of drugs which should be known as "cardio-vascular drugs and poisons,"* I have copied the following tabulated statement which belongs to Germain Sée, and will now read to you :

1. *Cardiac Musc.*.—Stimulation by digitalin, iodine in small doses, camphor, caffeine; paralysis by digitalin in the second period of action, emetin, salts of copper, barium and potassium, chloral in large doses, scillain.
2. *Intra-Cardiac Muscular Motor Centres.*.—Stimulation not given; paralysis by saponin in its last period of action, iodine in large doses.
3. *Intra-Cardiac Inhibitory Centres.*.—Stimulation by muscarine; paralysis by atropine, fabarine, sparteine in large doses.
4. *Intra-Cardiac Ramifications of the Inhibitory Filaments of the Vagus Nerve.*.—Stimulation by nicotine, pilocarpine, calabar bean; paralysis by pilocarpine, second phase of action.
5. *Trunk of the Vagus Nerve.*.—Stimulation by aconitine, nepaline; paralysis by sparteine; nepaline, second phase of action.
6. *Accelerator Filaments of the Great Sympathetic.*.—Stimulation by apomorphine; paralysis by sparteine.
7. *Medullary Inhibitory Centres.*.—Stimulation by digitalin; paralysis by chloral.
8. *Vase-Motor Centres.*.—Stimulation by bromide of potassium; paralysis by croton chloral; hydrocyanic acid.

In this long list it will be remarked there is no mention of convallaria, but as we are aware already, it may be properly approximated, at least so far as our actual knowledge extends, with digitalin; it is possibly, therefore, a simulator of the cardiac muscle in its first period of action, whilst its after effects may become of a paralytic order. Further, it is, after the manner of digitalin, a stimulator of the medullary inhibitory centres. It is no doubt, in this latter action, that resides its special power to control dyspnoea and the symptoms of purely functional heart disorder, particularly paroxysmal palpitation and rapid and irregular heart-action dependent upon debility (Trideau).

To this I would add, it is probable that convallaria majalis is more potent in its action upon the pneumogastric trunks than it is in its direct influence over the cardiac muscular fibres. This appears to me a fair deduction from what I have noticed with respect to its action in my cases. In regard to caffeine, I am of opinion that it is mainly through its elective action upon granular renal epithelium, which it stimulates in a remarkable degree, when it is in a healthy state, that it strengthens, indirectly, cardiac contractility. In

*New York Medical Journal, March 10, 1883, p. 279.

addition, it contributes to this result, by a moderate, stimulating action upon the different sources of nerve supply of the heart.

In terminating this clinical study of the action and uses of caffeine and convallaria, I am led to ask, with a late writer, why it is that neither it nor experimental physiology has yet yielded the fruits which might have been expected from them, in regard to the elective action which certain therapeutic, or toxic substances from the vegetable kingdom, exercise on one or the other parts of the apparatus of cardiac innervation.

As it has been stated elsewhere, there are probably two special reasons which may serve to explain this.* The first lies in the complexity of the composition of these alkaloids, *i. e.*, aconitine, digitalin, pilocarpine, which probably contain many distinct active principles, possessing absolutely dissimilar pharmacodynamic properties. The second is, that the localization of the effects of the same agent varies with the doses and duration of the experiment, *i. e.*, effects of the drug are described without indicating the precise circumstances under which they were produced.

"Moreover, these primitive and specific effects of a drug on a certain part of the apparatus of the innervation of the heart, may be masked or interfered with by the energetic effects of the same agent on other systems."

*Summary of Cases Seems to Show:—*1. In caffeine and convallaria we have two efficient heart tonics.

2. Diuretic action of caffeine is more marked than that of convallaria.

3. Convallaria is well borne by the stomach of most patients suffering with chronic cardiac disorders.

4. When not well supported, rejection of medicine by the stomach is probably due to the uræmic condition already commencing.

5. As cardiac tonics it is difficult, as yet, to assign a decided superiority to either of these drugs, they both giving increased cardiac power.

6. Cumulative effects do not occur from their continued use during a period of ten days or more.

7. Their power of restoring the rhythm to the cardiac pulsations, and increasing the bulk of urine, is not equal to that of the infusion of digitalis.

8. In this latter drug we have still the most efficient heart tonic and regulator which has been discovered.

9. Digitalis is a more powerful diuretic than caffeine.

*The British Medical Journal, February 17, 1883, p. 319-20.



